

REVIEW ON BLOOD CLOTTING ACTION OF NANOFIBER FROM BIOPOLYMERS

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ABSTRACT

Hemorrhage is the leading cause of death. Potentially preventable death. Improving our ability to control hemorrhage may represent the next major hurdle in reducing trauma mortality. New techniques and fibers for hemorrhage control are being developed and applied across the continuum trauma care such as hospital or other medical facility.

Keywords: blood clotting, nanofibres, biomaterials,

Trauma, hemostatic.

1. INTRODUCTION

This paper, generally reviews the literature on blood clotting action on nanofibers from biopolymer. It indicates varying degrees of efficacy based on product utilized, blood clotting, function of nanofiber and educational methodologies used for implementation by military and emergency medical service¹. Hemorrhage occurs when primary and secondary hemostasis fails to stop blood loss. Trauma deaths are a result of hemorrhage in 37% of civilians and 47% military personnel and the primary cause of death for individuals under 44 years of age. New techniques and biopolymers used to treat hemorrhage are inadequate for severe bleeding. Several hemostatic products are currently used or under development. Cyanoacrylates are utilized as hemostatic aids in oral surgery but can cause inflammation. Gelation- resorcinol-formaldehyde glue was frequently used as a sealant and yields excellent tensile strength but has less clotting ability. Quick clot speeds clot formation by creating an

exothermic reaction when absorbing water¹⁹. Compared to other sealants. The coagulation cascade describes the components of blood and how they are involved in the process of clot formation as the cascade becomes activated, the blood progress from non clotting to clotting state, causing changes in both molecular charge states and effective change mobility²⁰. The final step of the cascade involves two components, thrombin and fibrinogen. Thrombin acts by cutting the fibrinogen, forming fibrin filaments-which spontaneously aggregate. The end of clotting time has been defined as the time at which a fibrin clot is formed³. Uncontrolled hemorrhage was similar in all animals in both models and was immediately controlled with the application of either dressing¹⁸. Rapid trauma hemostat was developed using nanoengineering inorganic nanofibers.

2. HAMOSTATIC CONTROL

Hemorrhage is the leading causes of death from 1-34 years and the fifth leading cause of death overall in USA, with uncontrolled hemorrhage being the leading causes of potentially preventable death. Improving our ability to control hemorrhage may represent the next major hurdle in reducing trauma mortality. New techniques, devices, and drugs for hemorrhage control are being developed and applied across the continuum of trauma care. Prehospital emergency room and operative and critical care.

Animal models have played a crucial role in hemorrhagic shock research. Almost all advances and

interventions in hemorrhage have been initially or concomitantly described in such models. There adhesives basically three major types experiential models for hemorrhage shock: fixed volume hemorrhage, fixed pressure hemorrhage, and uncontrolled hemorrhage. Some models use a combination of strategies even though they provide distinct hemodynamic and hemostatic responses⁹. The animal experiments were performed according to the protocol approved by the university ethics committee, the hemostatic function of young and old platelets and the survival time have been examined in rabbits modals⁵. Currently represent the limit of modern trauma surgery. These maneuvers may soon be replaced by one or, more likely, a combination of the hemostatic drugs, fibrin, foams, and dressings currently being developed and evaluated¹⁰.

Surgeons have an array of option to control bleeding, including, mechanical and thermal techniques and devices as well as pharmacotherapy and topical agents (Table.1).

TABLE 1

2.1 Techniques for Maintaining Hemostasis³

Mechanical techniques

- Direct pressure
- Sutures
- Staples
- Ligating clips
- Fabric pads
- Gauzes
- Sponges
- Blood component/ replacement therapy

Thermal techniques

- Electrocautery
- Hemostatic scalpel
- Laser

Chemical Techniques

Pharmacotherapy

- hypotensive anesthesia
- epinephrine
- vitamin k
- protamine
- desmopressin
- aminocaproic acid
- tranexamic acid

Topical Hemostats

- collagen
- cellulose
- gelatins
- thrombin
- topical sealants and adhesives
- fibrin
- synthetic glues

TABLE 2

2.2 Factors contributing to intraoperative bleeding³

- Exposed bone
- Diffuse capillaries
- Unseen sources of bleeding
- Surgical incisors
- Tissues not amenable to suturing
- Low pressure suture lines
- Stripped adhesions
- Anticoagulant medications
- Coagulopathies and platelet dysfunction

TABLE 3

2.3 Advantages of effective hemostasis during surgery³

- Fewer Transfusions
- Better visualization of surgical field
- Reduced surgical time
- Decreased morbidity and death

Rapid and effective hemostasis allows the surgeon to retain visualization of the surgical field. This can both reduce the procedure time and the risk of accidental injury. In turn, a reduction in surgery time may lead to potential savings. Effective hemostasis

also should decrease the morbidity³. Coagulopathy resuscitation practice focuses primarily on rapid reversal of acidosis and prevention of hypothermia while concurrent surgical interventions focus on controlling hemorrhage and contamination¹¹.

3. HEMOSTATIC FUNCTION

The mechanism of hemostasis and thrombosis is critical to the management and stabilization of a patient undergoing any surgical procedure. Hemostasis can be defined as a tightly regulated process that maintains the blood flow through the vasculature simultaneously as a thrombotic response to tissue damage occurs. Maintaining hemostasis requires a complex interaction of the vessel wall, platelets, coagulation, and the fibrinolytic systems³.

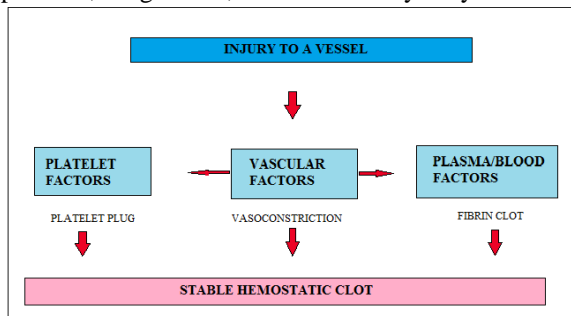


Figure 1 The synergy of factors that contribute to normal hemostasis³.

After the injury occurs, there is a temporary local contraction of vascular smooth muscle and the blood flow slows, promoting platelet adhesion and activation within 20 seconds of the injury, circulating von willebrand factors attaches to the sub endothelium at the site of injury and adheres to the glycoprotein on the surface of platelets. As the platelets adhere to the injury surface, they are activated by contact with collagen-exposing receptors that bind circulating fibrinogen is formed³. the coagulation cascade is a series of dependent reactions involving several plasma proteins, calcium ions, and platelets that led to the conversion of fibrinogen to the conversion of fibrinogen to fibrin. (Figure 1).

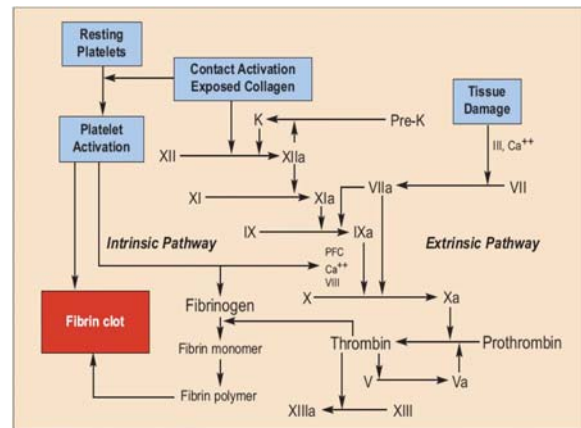


Figure 2 The clotting cascade. Thrombin catalyzes the conversion of fibrinogen to fibrin, one of the last steps of the coagulation cascade³.

3.1 intrinsic pathway

The intrinsic pathway, which is triggered by elements that lie within the blood itself (intrinsic to the blood), occurs in the following way. Damage to the vessel wall stimulates the activation of a cascade of clotting factors (for the sake of simplicity we will not consider the individual factors). This cascade results in the activation of factor X. Activated factor X is an enzyme that converts prothrombin to thrombin. Thrombin converts fibrinogen to fibrin monomers, which then polymerize in fibrin fibers. Fibrin fibers form a loose meshwork that is stabilized by cross links created by factor XIII. The stabilized meshwork of fibrin fibers is now a clot that traps red blood cells and platelets and thus stops the flow of blood.

3.2 Extrinsic Pathway

The extrinsic pathway is triggered by tissue damage outside of the blood vessel. This pathway acts to clot blood that has escaped from the vessel into the tissues. Damage to tissue stimulates the activation of tissue thromboplastin, an enzyme that catalyzes the activation of factor X.

3.3 Clotting of blood

The blood contains about a dozen of clotting factors. These factors are proteins that exist in the blood in an inactive state, but can be called into action when tissues or blood vessels are damaged. The activation of clotting factors occurs in a sequential manner. The first factor in the sequence activates the second factor, which activates the third factor and so on. This series of reactions is called the clotting cascade. Blood clotting is the transformation of liquid blood into a semisolid gel. Clots are made from fibers (polymers) of a protein called fibrin (see the diagram below). **Fibrin** monomers come from an inactive precursor called **fibrinogen**. The body of the fibrinogen molecule has caps on its ends that mask fibrin-to-fibrin binding sites. If the caps are removed then fibrin monomers polymerize to form fibrin polymers. This process requires **thrombin**, the enzyme that converts fibrinogen to fibrin. This process also requires **calcium**, which acts as a kind of glue to hold the fibrin monomers to each other to form the polymeric fiber. The fibrin fibers form a loose meshwork that is stabilized by clotting factor **XIII**. The stabilized meshwork of fibrin fibers traps erythrocytes, thus forming a clot that stops the flow of blood.

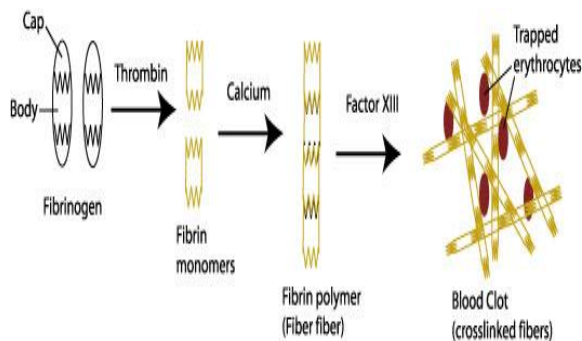


Fig.3. Clotting of Blood.

The hemostatic function was measured by performing serial ear bleeding times in irradiation induced thrombocytopenic rabbits⁵. The clot structure was also characterized by measuring the platelet contractile force and elastic modulus of polymerizing fibrin and cellular components. This system applies a calibrated compressive force periodically to an

aliquot of whole blood undergoing thrombin-initiated clotting⁶. The novel microfluidic method to detect the coagulation time by the measurement of the transmitted light intensity, potentially allowing blood coagulation measurement easily in the clinical setting. Then the other historical lab methods used to measure the blood clotting such as tilt tub method and wire loop method⁸.

4. HEMOSTATIC AGENTS

The study of hemostatic agents and their applicability in the out of hospital setting has primarily focused on the during military operations and limited implementation with the civilian emergency medical systems. The use for control bleeding is documented as early as ancient Egyptian culture. Where fresh meat was utilized as an efficient hemostatic and mechanical agent. More recent products have been developed with varying efficacy, with the foundation for utilization outside of the hospital environment predominally dived from animal studies and case reports . the active development and evaluation of alternative pressure type pressure desiring such as Biohemostat, chitosan and fibrin hemostatic agents. With hemostatic agents, various compounds are utilized to facilitate coagulation at the site of the injury. Hemostatic agents to treat or prevent bleeding. The effectiveness of these agents is measured in time to hemostasis based on the type and severity of the injury. The two primary agents being investigated either add a substance to a wound which increase the concentration of local clotting factors with chitosan, a naturally occurring, biocompatible polysaccharide derived from shrimp shells, or by increasing the availability of clotting factors with fibrin¹. Both types of agents serve to facilitate the formation of clot at the site of the injury through direct application. Currently, the utilization of hemostatic agents has been predominantly limited to researchers. The Quick clot, a zeolite works by absorbing water and concentrating coagulation factors to stop bleeding in a series of patients². The other hemostatic products to help control surgical bleeding when it is encountered. These agents range from the absorbable hemostats such as coagulation factors used for more extensive bleeding³. Absorbable topical hemostatic agents have since been developed and provide useful adjunctive therapy when conventional methods of hemostasis are ineffective or impractical . (Figure 4)³.

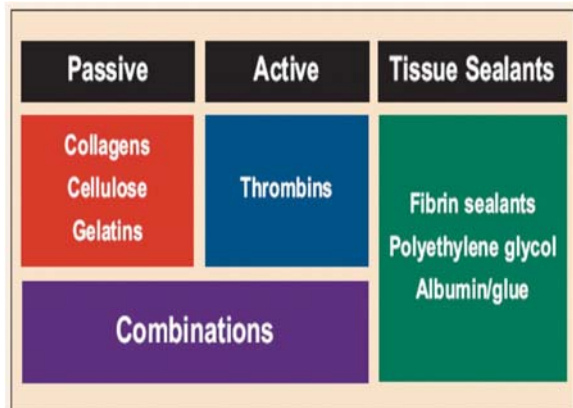


Figure4 Available topical hemostatic modifiers.

4.1 Passive hemostasis:

The basic mechanism of action of passive hemostatic agents is to provide a physical structure around which platelets can aggregate so a clots form. Passive topical hemostatic agents come in multiple forms and methods of application that can be important factors in determining their effectiveness. Gauze, sheets, sponges, and fleece are most popular among surgeons. Collagen-based products provide hemostasis through contact activation and the promotion of platelet aggregation, which occur as a direct result of contact between blood and the collagen. Cellulose-based products contain regenerated oxidized cellulose. They initiate clotting via contact activation; however, the exact mechanism is not completely understood.

4.2 Active hemostasis:

Active topical hemostatic agents have biological activity and directly participate at the end of the coagulation cascade to induce a clot at the site of bleeding. Active agents used in surgery include thrombin and combination products containing thrombin. Currently, there are three active topical hemostatic agents available on the US market as a single agent: Thrombin-JMI® (Thrombin, Topical, Bovine Origin, USP); Evithrom™ (Thrombin, Topical [Human], Omrix™ Biopharmaceuticals, Ltd); and Recothrom™ (Thrombin, Topical [Recombinant]; ZymoGenetics®, Inc)³. Nowadays increasing use of drugs in hamostatic medicine that inhibit platelets function or thrombin including clopidogrel, heparins, fondaparinux, and melagatran present the clinician with agents that may not be readily reversible with standard therapies⁴.

5.Hemostatic biopolymers:

Biomaterials have been used in both civilian and military settings with less exploration for the latter. One typical example is the biomaterials for hemorrhage control in surgery at hospital settings and for combat casualty care on battlefield . Tremendous advances in the area have been made for improvement of health care and life saving in civilian community and in military operations as uncontrolled hemorrhage from trauma is the second leading cause of death in the civilian community following central nerve system injuries and leading cause of death on the battlefield followed by brain injuries¹². Advances in hemostatic materials have been made in the past few years given the significant interests in hemorrhage control on battlefield¹².Biopolymers have a long history of using biomaterials for hemorrhage control. Typical hemostatic biopolymers include proteins (e.g., fibrinogen, thrombin, collagen, gelatin, albumin, and polysaccharides (chitosan, chitin, poly(Nacetyl glucosamine) and cellulose). They have been used in the forms of solid sheets/ sponges, powders and liquids.

5.1 Classification of hemostatic biomaterials¹²

TABLE 5.1

MATERIALS	MATERIAL TYPE	EXAMPLES
Solid sheets or sponges, particles/fibers	Bio polymers	Dry fibrin dressings with difference compositions, chitosan-based hemcon dressings, poly(N-acetyl glucosamine) based rapid deployment hemostats bandage, collagen, gelatin, oxidized cellulose, potato starch based microporous polysaccharide hemispheres, partially deacetylated chitin hydrochloride fibers.
	Synthetic polymers	Polycolic acid surgical felt and poly (2-hydroxyethyl methacrylate)
	ceramics	Zeolite and their derivatives (quikclot)

TABLE 5.2

Liquid sealants, dispersions	Polymer- ceramic composites	Chitosan-silica dressing, granular combination of alginate and Ag ⁺ Zn ²⁺ -exchanged zeolite, granular combination of smectite mineral and polyacrylate
	Biopolymers	Fibrin sealant and foam, chitosan and poly(N-acetyl glucosamine) gels, chitosan adhesives.
Liquid sealants, dispersions	Synthetic polymers	Polyethylene glycol sealants.
	Bio-synthetic polymers	Gelatin-poly(L-glutamic acid) glues

6. IMPORTANCE OF NANOFIBER MATERIALS IN HEMOSTATIC FUNCTION

Nanofiber process has increased in recent years, and this technology has been exploited for a wide range of applications. Among various nanomembrance wound dressing and self assembly. Nanofiber have very large surface area to volume ratio and flexibility in surface, these properties make the polymer nanofiber use in many important medical application. Nanofiber achieve good result on properties required for wound dressings, because of its nano-size structure. In the past decade, humorous studies revealed the areas in which nanofiber production, which established a starting step in the development of a new generation of textile products in medical application¹³. Electrospinning is the only method capable of producing continuous polymer nanofiber¹⁴. The effectiveness of nanofiber micro-dispersed oxidized cellulose with gentamicin was proved according to culture findings. The positive influence of the products on wound healing and a good hemostatic effect was conformed¹⁵ and the nano coating of oxides to stop bleeding more particularly, to ultra thin layers of oxides on the surfaces of materials to provide effective control of bleeding¹⁶. Use of a layer as thin as a few atomic layers to as thick as hundreds of nanometers of silica, a silicate or another effective oxide on a verity of surface/material to scaffold, with a water content of over 99.5% . These leads to the establishment of a nanofiber barrier that can be used to achieve complete hemostatis in less than 20 s in multiple tissue and in a variety of different wounds¹⁷. Nanofiber structure of self-assembling peptids has been studied extensively, but the molecular mechanisms underlying self-assembly and reassembly, gauze with nanoparticles, giving it a vastly improved ability to Holt blood loss. The material could help save lives on the battlefield and in civilians situations, where trauma victims often bleed to death before they can be transported to a hospital or other medical facility.

7. CONCLUSION

This paper deals with the blood clotting action of nanofiber from biopolymers. The hemorrhage probably controls more blood loss. It

discussed about the hemostatic function, uses of nanofiber in hemorrhage and hemostatic polymers. The fast and effective blood management plan incorporating topical hemostatic agents may be essential for achieving optimal patient outcomes. Familiarity with the materials and products to achieve hemostatis and their preparation can facilitate their optimal use. With the appropriate and correct use of these materials has the potential to improve outcomes for patient, the surgical team and health care facilities.

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BIOGRAPHIES



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